

of the PROSPECT (Predictors of Response to CRT) trial as well as the role of the sponsor, Medtronic, that require clarification and correction. The author claims that study sites were selected solely because they were high-volume cardiac resynchronization therapy (CRT) implantation centers rather than on the basis of echocardiographic experience. The PROSPECT trial included academic and large private practice centers in Europe, the U.S., and Hong Kong. The CRT implantation experience was 1 criterion for selection, because placement of the left ventricular lead is viewed as an important contributor to therapeutic response. Additional and equally important criteria included cooperation among echocardiography, electrophysiology, and heart failure specialties within the center; the ability to collect standard echocardiography data; and a demonstrated ability to execute clinical trials. Furthermore, sites were accredited by their regional core echocardiography laboratory by providing high-quality images before enrolling subjects (2).

Contrary to Sanderson's statement (1), enrolling centers were not required to analyze tissue Doppler imaging (TDI); this was the responsibility of the core echocardiography laboratories (2). Hence, training the centers to analyze tissue Doppler images was not necessary. The PROSPECT trial was not originally powered to assess the validity of TDI measures, and as such, sites were not required to have echocardiography machines with this capability. During the study but before any analysis, Medtronic supported the physician Steering Committee's request to expand the enrollment of patients at centers with TDI-capable equipment, to properly power the study for analysis of TDI parameters. Enrollment was increased from an originally planned 300 subjects to 498. The Steering Committee—comprising prominent echocardiographers, heart failure specialists, and electrophysiologists—was involved in the trial design and the collection, monitoring, and analysis of data (3). Throughout the execution of the trial, the sponsor followed their recommendations, which included a quality control initiative to ensure consistent measurements of images by the core laboratories (2).

*Dan Schaber, PharmD

*VP CRDM Clinical Research
Medtronic, Inc.
8200 Coral Sea Street Northeast MVS33
Mounds View, Minnesota 55112
E-mail: dan.schaber@medtronic.com

doi:10.1016/j.jacc.2009.06.053

Please note: Dr. Schaber is the Vice President of Clinical Research of Medtronic Inc.

REFERENCES

1. Sanderson JE. Echocardiography for cardiac resynchronization therapy selection—fatally flawed or misjudged. *J Am Coll Cardiol* 2009;53:1960–4.
2. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. *Circulation* 2008;117:2608–16.
3. Yu CM, Abraham WT, Bax J, et al. Predictors of response to cardiac resynchronization therapy (PROSPECT)—study design. *Am Heart J* 2005;149:600–5.

Reply

I thank Dr. Schaber for his clarifications and comments on my commentary (1). I have no doubt that the PROSPECT (Predictors of

Response to CRT) trial was designed with the best of intentions, but sometimes there are unforeseen and unintended consequences of clinical trials. The importance of centers having implantation experience is clearly a *sine qua non*, but my point was that the echocardiography experience at these centers might not have been so critically evaluated. This is illustrated by Dr. Schaber's statement that "enrolling centers were not required to analyze tissue Doppler imaging (TDI); this was the responsibility of the core echocardiography laboratories. . .hence, training the centers to analyze tissue Doppler images was not necessary." This might be strictly true, but technical skill is required for the acquisition of the TDI images as well as analysis. It is clear from the study design report (2) that TDI measurements were a critical part of the study from the start (see Table 1 of the article, which lists all the standard and TDI indexes to be tested). In addition, it was intended that these would be a major part of the study: page 601: "We will test each echocardiographic predictor against predetermined primary and secondary response outcome measures, each with predefined cutoff values." In light of this, it is surprising that Dr. Schaber states "The PROSPECT trial was not originally powered to assess the validity of TDI measure, and as such, sites were not required to have echocardiography machines with this capability." Indeed, one of the problems in retrospect was the lack of power. A large number of echocardiographic predictors were evaluated, but individual sample sizes were not calculated; rather, power calculations were done on an initial sample size of 250 patients, but there is no justification of how this number was decided upon. Furthermore, if there is wide variation in the ability to acquire high-quality images, then analysis will be difficult no matter how good the training is, and this will affect the power of the study—as subsequently became obvious in the published results (3). For example, even the results of the relatively simple measurement of left ventricular volume were often widely different in the implanting centers compared with the core laboratories, as I pointed out in my commentary. Thus, a potentially useful tool has been discredited and now practically all but discarded, which might not be in the best interest of potential patients or the community paying for the excess number of implanted devices.

*John E Sanderson, MD

*Birmingham University
Cardiovascular Medicine
The Medical School
University of Birmingham
Birmingham, West Midlands B15 2TT
United Kingdom
E-mail: jesanderson@hotmail.com

doi:10.1016/j.jacc.2009.08.025

REFERENCES

1. Sanderson JE. Echocardiography for cardiac resynchronization therapy selection—fatally flawed or misjudged. *J Am Coll Cardiol* 2009;53:1960–4.
2. Yu CM, Abraham WT, Bax J, et al. Predictors of response to cardiac resynchronization to therapy (PROSPECT)—study design. *Am Heart J* 2005;149:600–5.
3. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. *Circulation* 2008;117:2608–16.